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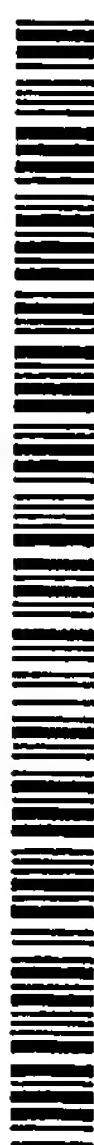
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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



**WO 01/26702 A3**

(54) Title: NITRIC OXIDE-MODIFIED LINEAR POLY(ETHYLENIMINE) FIBERS AND USES THEREFOR

(57) Abstract: A novel coating for medical devices provides nitric oxide delivery using nanofibers of linear poly(ethylenimine)diazoniumdiolate. Linear poly(ethylenimine)diazoniumdiolate releases nitric oxide (NO) in a controlled manner to tissues and organs to aid the healing process and to prevent injury to tissues at risk of injury. Electrospun nanofibers of linear poly(ethylenimine)diazoniumdiolate deliver therapeutic levels of NO to the tissues surrounding a medical device while minimizing the alteration of the properties of the device. A nanofiber coating, because of the small size and large surface area per unit mass of the nanofibers, provides a much larger surface area per unit mass while minimizing changes in other properties of the device.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/27769

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61L27/54 A61L27/34 A61L29/16 A61L29/08 A61L31/16  
A61L31/10 A61L17/14 A61L15/44 A61L15/26

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L A61F D01D D04H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, COMPENDEX, CHEM ABS Data, EMBASE, INSPEC

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PULFER SHARON K ET AL: "Incorporation of nitric oxide-releasing crosslinked polyethyleneimine microspheres into vascular grafts." JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, vol. 37, no. 2, 1997, pages 182-189, XP000978327 ISSN: 0021-9304 the whole document	1-5, 10, 11, 22-24
Y	---	6-9 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

10 April 2001

Date of mailing of the international search report

23.04.2001

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**INTERNATIONAL SEARCH REPORT**

Interr. 1st Application No

PCT/US-00/27769

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DOSHI J ET AL: "Electrospinning process and applications of electrospun fibers" JOURNAL OF ELECTROSTATICS, AUG. 1995, NETHERLANDS, vol. 35, no. 2-3, pages 151-160, XP000971801 ISSN: 0304-3886 page 152, paragraph 3 page 159, paragraph 1 - paragraph 2 ---	6-9
X	SMITH DANIEL J ET AL: "Nitric oxide-releasing polymers containing the (N(O)NO)- group." JOURNAL OF MEDICINAL CHEMISTRY, vol. 39, no. 5, 1996, pages 1148-1156, XP002157493 ISSN: 0022-2623 page 1151, column 2 -page 1152, column 2 ---	1-5, 10, 11, 22-24
Y	WO 98 03267 A (ELECTROSOLS LTD ;COFFEE RONALD ALAN (GB)) 29 January 1998 (1998-01-29) page 2, paragraph 2 -page 4, paragraph 3 figures claims ---	12-21
X	WO 96 32136 A (US GOVERNMENT ;UNIV AKRON (US)) 17 October 1996 (1996-10-17) example 3 page 16, line 19 -page 17, line 25 ---	1, 2, 10, 11
A	US 4 043 331 A (COCKSHOTT IAN DEREK ET AL) 23 August 1977 (1977-08-23) cited in the application column 2, line 9 - line 34 column 3, line 16 - line 43 claims ---	1, 12
A	BAUER JOSEPH A ET AL: "Evaluation of linear polyethyleneimine/nitric oxide adduct on wound repair: Therapy versus toxicity." WOUND REPAIR AND REGENERATION, vol. 6, no. 6, November 1998 (1998-11), pages 569-577, XP000978321 ISSN: 1067-1927 the whole document ---	1-5, 10, 11, 22-24
A	US 5 024 789 A (BERRY JOHN P) 18 June 1991 (1991-06-18) claims ---	12 -/-

## INTERNATIONAL SEARCH REPORT

Internat'l Application No

PCT/US 00/27769

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 18893 A (UNIV DREXEL ;KO FRANK K (US); LAURENCIN CATO (US); ALLEGHENY HEALT) 22 April 1999 (1999-04-22) page 7, line 23 -page 8, line 8 page 9, line 12 - line 24 -----	12
A	US 5 376 117 A (MAURIN ANNE A ET AL) 27 December 1994 (1994-12-27) abstract -----	12

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/27769

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 22-24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-11,22-24

A medical device coated with nanofibers of a polymeric nitric oxide donor.

2. Claims: 12-21

A process of making a medical device by coating the medical device with nanofibers of poly(ethylenimine) by subjecting said polymer to an electric field.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/27769

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9803267 A	29-01-1998	AU 3628497 A EP 0912251 A JP 2000516130 T		10-02-1998 06-05-1999 05-12-2000
WO 9632136 A	17-10-1996	US 5691423 A AU 695579 B AU 5448396 A CA 2216696 A EP 0822833 A JP 11503456 T		25-11-1997 13-08-1998 30-10-1996 17-10-1996 11-02-1998 26-03-1999
US 4043331 A	23-08-1977	GB 1527592 A CA 1090071 A DE 2534935 A FR 2281448 A IT 1044659 B JP 1327858 C JP 51040476 A JP 60043981 B SE 423489 B SE 7508781 A US 4878908 A US 4044404 A		04-10-1978 25-11-1980 19-02-1976 05-03-1976 21-04-1980 30-07-1986 05-04-1976 01-10-1985 10-05-1982 06-02-1976 07-11-1989 30-08-1977
US 5024789 A	18-06-1991	NONE		
WO 9918893 A	22-04-1999	AU 1075699 A US 6106913 A		03-05-1999 22-08-2000
US 5376117 A	27-12-1994	NONE		